



Association of Lung Cancer and Tuberculosis: A Cross Sectional Study from Northwest of Iran

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Abstract

Background: Tuberculosis (TB) is a life-threatening disease, which still remains a major public health concern in Iran, as the country is an endemic region for TB. On the other hand, carcinoma of the lung is the most common and lethal cancer. As the lung cancer involves respiratory system, it has many common connections with TB, too, and it is likely that immunosuppressant drugs, like the ones used in cancer treatments, increase the risk of TB development.

Objectives: To assess the possible association of TB and lung cancer, the current study evaluates the incidence of TB among patients with lung cancer.

Methods: In the present cross-sectional study, patients with diagnosis of lung cancer were selected from the referral centers between 2011 and 2016. The TB among the patients was diagnosed, using radiographic pulmonary infiltration, *M. tuberculosis* culturing, and sputum smear. The diagnostic tests were done twice to certify the results.

Results: From 845 cases entering the study, 9 patients (1.1%) were diagnosed with TB and the smear test was positive in 5 patients. The cases aged between 40 and 67 years old, with the mean age of 53.92 ± 8.02 . Women had a significantly more average age than men and adenocarcinoma was the most common type of lung cancer with a rate of 57.63%.

Conclusions: According to results of current study, there was a relationship between lung cancer and TB, while the incidence of TB in patients with lung cancer was more than the normal average rate of TB incidence in the region.

Keywords: Lung Cancer, Smear Test, Tuberculosis, Iran

1. Background

Lung carcinoma is the most common carcinoma, implicating more than 1.6 million individuals annually (1). With the 5-year survival rate of 17.7 %, it represents fatal than any other leading cancer site (2). The remarkable fact about lung carcinoma is that the increased incidence with a large number of patients with lung cancer leads to a high mortality rate. It is known that smoking, exposure to chemicals like asbestos, arsenates, and some aromatics result in the pathology of lung cancer (3). Hereditary background and dietary factors have also been introduced as potential risk factors (4). Chemotherapy is the main treatment for most of the patients with lung cancer. Also, thoracic radiation therapy is used to cure as well. Most early-

stage patients undergo surgery, and 25% of the surgeries are followed by chemotherapy or thoracic radiation therapy, resulting in diminished immune system functions (5).

On the other hand, Tuberculosis (TB) is known as a threatening disease with a high rate of morbidity, as near one-third of individuals around the world are infected with *Mycobacterium tuberculosis* (6). It is still considered as a major health problem in developing countries like Iran, as the country is known as an endemic region for TB (7). During the last 20 years, it has become obvious that communal efforts to irradiate TB will remain to encounter a key challenge with the pervasive dissemination of drug-resistant tuberculosis strains (8). As the most important risk factors, poor living or working conditions and development of the factors, which impair the immune system, items like age,

gender, substance use, nutrition status, and malignancies are mainly considered as direct and underlying threats (9). As a predictable consequence, the immunosuppressive effects of cancer treatments, especially chemotherapy, can lead to a higher risk of developing TB.

Inflammatory lung diseases, such as sarcoidosis (10), asthma (11), and chronic obstructive pulmonary disease (12) are strongly linked to lung cancer involvement. A probable relationship between result in the pathology of lung cancer and TB infection has been reported formerly (13). Various studies indicated that both diseases have got some common immune escape mechanisms in development and pathogenesis (14, 15). As it could be predicted, some complications of the cure path of cancer, such as chemotherapy, can lead to an impaired immune system, which makes the individual more prone to catching infectious diseases like TB. Although lung cancer and TB have common clinical correspondences (16), in fact, no clear association has been established (17).

2. Objectives

Therefore, the current study was conducted to assess the prevalence of TB among patients with lung cancer and discuss the possible relation between TB and lung cancer.

3. Methods

3.1. Study Design and Population

In the present cross-sectional study, all the patients, who were referred to educational-medical centers of Tabriz University of Medical Sciences (Tabriz, Iran) between March 2011 and March 2016 with diagnose of lung cancer, were included in the study regardless of their type of lung cancer by convenience sampling. Exclusion criteria consisted of patients with a lack of definitive diagnosis, history of previous TB infection, other ongoing pulmonary diseases, and neutropenia.

Clinical data were obtained from the patients' medical records, using the hospital information database. All patient medical cases were checked and demographic information like age and gender were obtained. Based on information provided in patients' medical records, items including the smear result and affliction to TB, type of lung cancer and history of smoking were obtained. Patients with incomplete information were contacted via phone for further information. As the data were acquired from major referral centers, and by considering the geographical properties of the area, the results could be generalized to the whole northwest of the country.

3.2. Diagnosis of Tuberculosis

Patients were diagnosed through radiographic pulmonary infiltrations and *M. tuberculosis* culture from patients' sputum samples was diagnosed by being cultured, using BACTEC™ MGIT™ (Mycobacteria Growth Indicator Tube) 960 system (BD Inc; Sparks, MD, USA) for 6 weeks. Sputum smears were classified as negative (culture-positive), scanty (1 - 9 bacilli/100 fields), ++ (1 - 9/field), or +++ (≥ 10 /field). In order to increase accuracy, the TB diagnostic tests were double checked.

3.3. Statistical Analysis and Ethical Considerations

The data were analyzed, using SPSS V.16 statistics software (SPSS Inc., Chicago, IL, USA). The data were represented as mean \pm standard deviation and percentage. The variables were compared, using independent *t* test for quantitative and chi-square for dichotomous ones. P value less than 0.05 was considered as significant.

The study protocol was approved by Regional Ethics Committee of Tabriz University of Medical Sciences (Tabriz, Iran) by the number of 94/1-10/3, which was in compliance with Helsinki Declaration.

4. Results

Of 845 patients, who were entered to the study, 729 were men (86.3%) and 116 were women (13.7%). The mean age and important characteristics of each group are mentioned in Table 1. With the mean age of 53.92 ± 8.02 , the statistical society was outspread between 40 and 67 years old. The mean age in women was significantly more than men ($P < 0.001$). The relation between TB and age, and TB and gender were not significant. Of the total of 845 patients, 649 patients (76.8%) were diagnosed with non-small cell lung cancer, including 487 patients (57.6%) with adenocarcinomas. Regarding smoking status, 200 patients (23.7%) were non-smokers, among whom 114 were women and 86 were men. More details on patients' gender, lung cancer type, history of smoking, and habitation are discussed in Table 1. In explanation of TB and lung cancer accompaniment, according to patients' medical records, TB was verified in 9 patients (1.1%), in which 5 patients' (0.6%) smear test was positive. Of all TB positive patients, 6 (66.6%) were male and 6 (66.6%) had a positive history of smoking, indicating no statistically significant association between gender ($P = 0.08$) and smoking ($P = 0.47$).

5. Discussion

In the present study, the frequency of TB among patients with lung cancer was evaluated among 845 patients

Table 1. Demographic and Cancer Type Information of the Patients^a

Variables	Values
Gender	
Male	729 (86.3)
Female	116 (13.7)
Living site	
Rural	191 (22.6)
Urban	654 (77.4)
Age	
Male	53.24 ± 8.26
Female	56.32 ± 5.8
Total	53.92 ± 8.02
Positive history of smoking	
Male	643 (76.09)
Female	2 (0.23)
Total	645 (76.33)
Lung cancer type	
Adenocarcinoma	487 (57.63)
Squamous cell carcinoma	107 (12.66)
Large-cell carcinoma	55 (6.5)
Small-cell carcinoma	73 (8.63)
Undifferentiated carcinoma	123 (14.55)

^aData were shown as frequency (percentage) or mean ± standard deviation.

and the results showed 9 cases of TB-infected patients with an incidence of 1.1%. TB is still a health problem in Iran as it is known as an endemic country for TB (7). The prevalence of TB in the northwest of Iran is also under the effect of the migrations from the Republic of Azerbaijan, as a border neighbor. In addition, the free treatment of TB in Iran attracts many patients from Azerbaijan to Iran and, as a result, the possibility of transmission rises (18). Despite being endemic, the incidence rate of TB in Iran is 14 (per 100 000 population) and less than 50 in the northwest of Iran, which are way less than the global rate (140 per 100 000 population) (18-20). The most important reason for the lesser rate of TB incidence in Iran, despite being an endemic area, lies in the powerful screening and treatment programs; as the treatment success rate for TB Iran is between 85% and 100% (21). Therefore, the rate of TB incidence in the normal population of the area is 0.014%. The incidence of TB among the patients with lung cancer in this study was 1.1%, showing a remarkable increase in comparison with the normal population. So, the prevalence of TB is higher among patients with lung cancer.

Many studies have been conducted due to the com-

mon pathophysiology of TB and lung cancer. In a study accomplished in Canada, no significant relationship between TB and lung cancer was observed (22). Also, in a 9-year prospective study, which determined the relevancy between prior lung diseases and risk of lung cancer, again no significant relation was apperceived (23). On the other hand, some studies signposted that lung cancer and TB can occur consecutively or at the same time (17). For example, in a study discussing the role of pollutants and chronic lung diseases in developing lung cancer, the correlation between TB and lung cancer was confirmed (OR=3.82)(24). A systematic review debating the correlation between lung cancer and TB confirmed the impact of TB on adenocarcinoma, but the influence of TB on squamous cell carcinoma was declined (6). The impact of cancer on increasing cancer risk has been deliberated before in a study in comparison with US guidelines for the management of latent TB infection in patients with cancer (25), but the study was conducted just at the epidemiological point of view and focus on US region. A study of Tuberculosis' effect on lung cancer as a risk factor in Iran showed a positive relationship among them (26), but had many disadvantages that lowered justifiability of the study; such as the patients' group could be higher in number, the time period could be longer, a remarkable portion of patients was over 60 years old and most of them were under-educated, that obviously affects the incidence of inflectional diseases, and no impression of smoking was reported. According to health statistics, the incidence of TB in the northwest of Iran is less than 50 people in every 100 000, which is way lesser than the incidence of patients with lung cancer (18, 20). These results could play an important role in proving the importance of lung cancer screening and prevention programs.

Discussing the fundamental factors supporting this idea, it is important to check out why TB and lung cancer occur concerted. They have many common risk factors, such as smoking history, gender, age, and previous pulmonary diseases. Even the coexistence of TB and lung cancer has been previously reported (27, 28). Obviously, the weakness of the immune system due to heavy therapies in patients coping with cancer plays an important role in patients' predisposition in catching infectious diseases. For instance, Cisplatin is a common treatment in lung cancer, and it has confirmed positive effects on apoptosis stimulation, nephrotoxicity, myelotoxicity, and immunosuppression and it is clear that apoptosis and immunosuppression processes can modulate the immune system's capability in confronting infectious diseases like TB (29-33).

The data were obtained from referral centers, so that they were more likely to participate in screening programs. Despite benefiting from an adequate duration of study and a relatively large number of patients, this study

had some limitations, such as the lack of detailed information on the period of time that the patient with lung cancer was infected by TB (e.g. after the completing the therapies, during the chemotherapy, simultaneously), but it is obvious that these goals were far away from the study's ultimate perspective. Although the results of the current study endorsed the previous related ones, any difference in the results should be considered with geographical diversities and the discrepancy between periods of treatment. Further analytical studies may be conducted in different points of Iran to check the correlation of TB and lung cancer.

5.1. Conclusions

The present study was conducted to assess the prevalence of TB among patients with lung cancer. According to the results, the incidence of TB among patients with lung cancer was 1.1%, 0.6% of whom had positive Acid-Fast Bacilli smear test result. In comparison to the regular population of the country, with 14 people per 100 000 (0.014%), prior lung cancer can increase the risk of TB in patients.

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This study is resulted from a thesis registered at Tabriz University of Medical Sciences (Tabriz, Iran) with registration number of 94/1-10/3.

Footnotes

Authors' Contribution: Study concept and design: Parviz Saleh, Mehrnaz Ghaffari, and Mohammad Naghavi-Behzad; analysis and interpretation of data: Reza Piri, Mehrnaz Ghaffari, and Mohammad-Salar Hosseini; drafting of the manuscript: all of the authors; critical revision of the manuscript for important intellectual content: all of the authors; statistical analysis: Reza Piri and Mohammad-Salar Hosseini.

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Patient Consent: All participants gave informed consent before inclusion in the trial.

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